DNA Repair Changes with the Flip of a Switch

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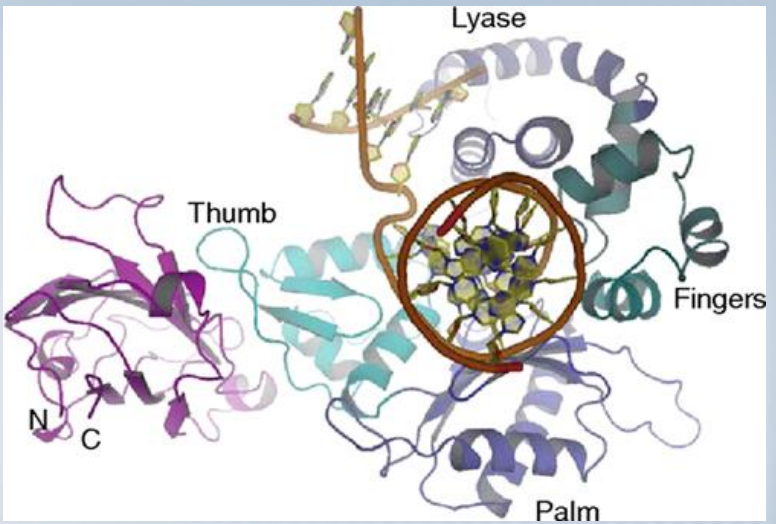
- The DNA blueprint in each human cell undergoes about 100,000 damaging events every day, each which requires a team of proteins to work together to fix the mutated DNA.
- In pursuit of a better fundamental understanding of DNA repair, researchers use small-angle x-ray scattering at NSLS to image a large, multi-part molecule called a scaffolding protein. The molecule, called XRCC1, orchestrates DNA repair by holding the other repair proteins together in a multi-molecule complex.
- The group studied a subsection of XRCC1 called the N-terminal domain, which interacts with DNA polymerase ß, a protein that actively repairs damaged DNA.
- They discovered that this interaction can change with the flick of a biological switch. The N-terminal domain contains a "disulfide switch," a potential bond whose formation changes the molecule's secondary structure.
- Discovering the disulfide switch's role would help improve scientists' understanding of how DNA repair works, which could lead to better treatments for disease.



Model of the complex formed by XRCC1's N-terminal domain (in purple), damaged DNA (in orange), and DNA polymerase ß (with component parts thumb, lyase, fingers, and palm labeled).

M.J. Cuneo, R.E. London, "Oxidation State of the XRCC1 N-terminal Domain Regulates DNA Polymerase ß Binding Affinity," PNAS,, ***107****(15), 6805 (2010).*

Work performed on NSLS beamline X9